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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: T. Mitaka, et al.

Examiner: S. E. Fernandez

Application No.: 10/676,292

Group Art Unit: 1651

Filed: October 1, 2003

Docket: 1285-7 PCT/CON

For: SMALL HEPATOCYTE-RICH
COLONIES, PROCESS FOR
PREPARING THE COLONIES,
PROCESS FOR MATURATING
THE COLONIES INTO LIVER
TISSUE AND METHOD OF
ESTIMATING EFFECTS OF
DRUG BY USING MATURED
SMALL HEPATOCYTE-RICH
COLONIES

Dated: August 18, 2005

Confirmation No.: 7064

I hereby certify that this correspondence is being deposited with the
United States Postal Service as first class mail, postpaid in an envelope,
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Dated: August 18, 2005

Signature: K.J. Goodhand/

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO RESTRICTION REQUIREMENT

Sir:

This is in response to the Office Action mailed August 4, 2005, a reply to which is due September 4, 2005. In the Office Action, the Examiner is requiring restriction to one of Groups I-IX below, which are alleged as being distinct inventions:

I: Claims 1 and 2, drawn to small hepatocyte-rich colonies, classified in class 435, subclass 370.

- II: Claim 3, drawn to a process for preparing small hepatocyte-rich colonies comprising the step of dividing isolated hepatocytes into a heavy fraction enriched with parenchymal cells and a light fraction enriched with non-parenchymal cells, and recovering the light fraction, classified in class 435, subclass 370.
- III: Claim 4, drawn to a process for preparing small hepatocyte-rich colonies comprising the step of dissociating colonies from a culture dish by reacting an enzyme or without reacting an enzyme on small hepatocytes forming the colonies to recover the small hepatocytes, classified in class 435, subclass 370.
- IV. Claims 5 and 6, drawn to a process for maturing small hepatocyte-rich colonies into a liver tissue comprising the step of adding an extracellular matrix to the medium containing the cultured small hepatocyte-rich colonies, classified in class 435, subclass 370.
- V. Claims 7-10, drawn to a process for maturing small hepatocyte-rich colonies into a liver tissue or preparing a liver tissue for transplantation, comprising the step of placing small hepatocyte-rich colonies on a bioabsorbable sheet, classified in class 435, subclass 370.
- VI. Claims 11, 15, 19, 21, 25, 27, 31 and 33, drawn to a method of estimating an effect of a chemical substance on a liver function *in vitro* using the small hepatocyte-rich colonies matured according to the process of claim 5, classified in class 435, subclass 6.
- VII. Claims 12, 16, 20, 22, 26, 28, 32 and 34, drawn to a method of estimating an effect of a chemical substance on a liver function *in vitro* using the small hepatocyte-rich colonies matured according to the process of claim 7, classified in class 435, subclass 6.

- VIII. Claims 13, 17, 23 and 29, drawn to a method of estimating an effect of a chemical substance on a liver function *in vitro* using the small hepatocyte-rich colonies matured according to the process of claim 5, wherein the induction or repression pattern of a gene is compared with an induction or repression pattern of the gene associated with a chemical substance having a known effect, classified in class 435, subclass 6.
- IX. Claims 14, 18, 24 and 30, drawn to a method of estimating an effect of a chemical substance on a liver function *in vitro* using the small hepatocyte-rich colonies matured according to the process of claim 7, wherein the induction or repression pattern of a gene is compared with an induction or repression pattern of the gene associated with a chemical substance having a known effect, classified in class 435, subclass 6.

The Examiner is also alleging that the application contains claims directed to the following species, which are alleged as being patentably distinct:

- (a) The drug-metabolizing enzyme genes of claim 27.
- (b) The drug-metabolizing enzyme genes of claim 28.
- (c) The drug-metabolizing enzyme genes of claim 29.
- (d) The drug-metabolizing enzyme genes of claim 30.
- (e) The drug-metabolizing enzyme genes of claim 31.
- (f) The drug-metabolizing enzyme genes of claim 32.

In particular, the Examiner is requiring a species election as follows:

If applicant elects Group VI, applicant is further required to elect a single disclosed species from each of (a) and (e) set forth above.

Application No.: 10/676,292
Amendment and Response dated August 18, 2005
Reply to Office Action of August 4, 2005
Docket No.: 1285-7 PCT/CON
Page 4

If applicant elects Group VII, applicant is further required to elect a single disclosed species from each of (b) and (f) set forth above.

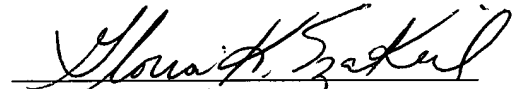
If applicant elects Group VIII, applicant is further required to elect a single disclosed species from (c) set forth above.

Finally, if applicant elects Group IX, applicant is further required to elect a single disclosed species from (d) set forth above.

In response to this restriction requirement, Applicants elect Group VI set forth above (claims 11, 15, 19, 21, 25, 27, 31 and 33). Applicants further elect "CYP3A2" as the gene for both (a) and (e) set forth above.

If the Examiner should have any questions or concerns regarding these elections, she is respectfully invited to contact Applicants' undersigned agent at the telephone number set forth below. Applicants respectfully request that consideration of the elected claims on the merits be commenced.

Respectfully submitted,


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